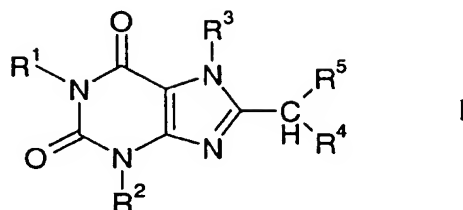


Claims

1. A compound of formula



in free or salt form, where

R¹ is hydrogen or alkyl optionally substituted by hydroxy, alkoxy, or alkylthio,

R² is hydrogen, alkyl, hydroxyalkyl, alkylcarbonyloxyalkyl, alkoxyalkyl, alkylthioalkyl, alkenyl, cycloalkylalkyl, heterocyclalkyl, aralkyl in which the aryl ring thereof is optionally fused to a 5-membered heterocyclic group or is optionally substituted by one or more substituents selected from alkoxy, amino, alkylamino, dialkylamino, acylamino, halogen, hydroxy, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, alkylsulfonylamino or dialkylaminosulfonylamino,

R³ is hydrogen or alkyl optionally substituted by hydroxy, alkoxy, or alkylthio,

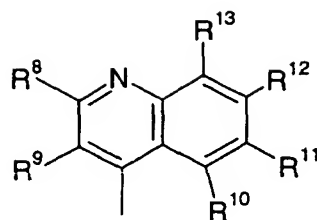
R⁴ is hydrogen or alkyl,

R⁵ is a quinolinyl, isoquinolinyl or oxodihydroisoquinolinyl group optionally fused to a 5-membered heterocyclic group and optionally substituted by one or more substituents selected from halogen, cyano, hydroxy, alkyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, alkoxy, alkylthio, alkenyl, alkoxycarbonyl, alkynyl, carboxyl, acyl, a group of formula -N(R⁶)R⁷, aryl optionally substituted by one or more substituents selected from halogen or alkoxy, or heteroaryl having 5 or 6 ring atoms attached through a ring carbon atom to the indicated carbon atom, and

R⁶ and R⁷ are each independently hydrogen or alkyl optionally substituted by hydroxy or alkoxy or one of R⁶ and R⁷ is hydrogen and the other is acyl, or R⁶ and R⁷ together with the nitrogen atom to which they are attached denote a 5- or 6- membered heterocyclalkyl group.

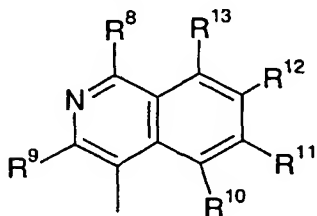
2. A compound according to claim 1, in which R⁵ is a quinolinyl group of formula

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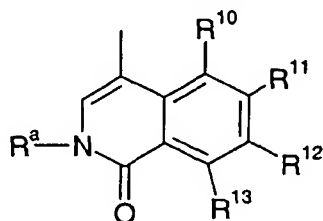
II

or an isoquinolinyl group of formula



III

or an oxodihydroisoquinolinyl group of formula



IIIA

where R^8 , R^9 , R^{10} , R^{11} , R^{12} and R^{13} are each independently hydrogen or a substituent selected from halogen, cyano, hydroxy, alkyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, alkoxy, alkylthio, alkenyl, alkoxycarbonyl, alkynyl, carboxyl, acyl, a group of formula - $N(R^6)R^7$, aryl optionally substituted by one or more substituents selected from halogen or alkoxy, or heteroaryl having 5 or 6 ring atoms, and R^6 and R^7 are as defined in claim 1, or R^{11} and R^{12} together with the carbon atoms to which they are attached denote a 5-membered heterocyclic group having two oxygen or nitrogen atoms in the ring, and R^a is hydrogen or C_1 - C_4 -alkyl.

3. A compound according to claim 1, in which

R^1 is hydrogen or C_1 - C_4 -alkyl optionally substituted by hydroxy, C_1 - C_4 -alkoxy or C_1 - C_4 -alkylthio,

R² is hydrogen, C₁-C₈-alkyl, hydroxy-C₁-C₈-alkyl, C₁-C₄-alkylcarbonyloxy-C₁-C₈-alkyl, C₁-C₄-alkoxy-C₁-C₈-alkyl, or C₁-C₄-alkylthio-C₁-C₈-alkyl, C₂-C₄-alkenyl, C₃-C₈-cycloalkyl-C₁-C₄-alkyl, heterocyclyl-C₁-C₄-alkyl where the heterocyclyl group is a 5- or 6- membered heterocyclyl group having one or two hetero atoms selected from nitrogen and oxygen atoms in the ring, phenyl-C₁-C₄-alkyl in which the phenyl ring is optionally substituted by one or more substituents selected from C₁-C₄-alkoxy, amino, C₁-C₄-alkylamino, di(C₁-C₄-alkyl)amino, C₁-C₄-alkylcarbonylamino, halogen, C₁-C₄-alkylsulfonylamino, or di(C₁-C₄-alkyl)aminosulfonylamino, and is optionally fused to a 5- membered heterocyclic ring having two oxygen or two nitrogen atoms in the ring,

R³ is hydrogen or C₁-C₄-alkyl optionally substituted by hydroxy, C₁-C₄-alkoxy or C₁-C₄-alkylthio,

R⁴ is hydrogen or C₁-C₄-alkyl,

R⁵ is a quinolinyl, isoquinolinyl or oxodihydroisoquinolinyl group optionally fused to a 5-membered heterocyclic group having two oxygen or two nitrogen atoms in the ring and optionally substituted by one or more substituents selected from halogen, cyano, carboxy, hydroxy, C₁-C₄-alkyl, hydroxy-C₁-C₄-alkyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-alkylthio-C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-alkylthio, C₂-C₄-alkenyl, C₂-C₄-alkynyl, C₁-C₄-alkylcarbonyl, a group -N(R⁶)R⁷ or phenyl optionally substituted by one or more substituents selected from halogen or C₁-C₄-alkoxy and

R⁶ and R⁷ are each independently hydrogen or C₁-C₄-alkyl optionally substituted by hydroxy or alkoxy, or one of R⁶ and R⁷ is hydrogen and the other is C₁-C₄-alkylcarbonyl, or R⁶ and R⁷ together with the nitrogen atom to which they are attached denote a 5- or 6-membered heterocyclyl group having one or two nitrogen atoms and, optionally, an oxygen atom in the ring.

4. A compound according to claim 2, in which

R¹ is hydrogen or C₁-C₄-alkyl, R² is hydrogen, C₁-C₈-alkyl, hydroxy-C₁-C₈-alkyl, or C₁-C₄-alkylcarbonyloxy-C₁-C₈-alkyl, C₂-C₄-alkenyl, C₃-C₆-cycloalkyl-C₁-C₄-alkyl, heterocyclyl-C₁-C₄-alkyl where the heterocyclyl group is a 5- membered heterocyclyl group having one nitrogen or oxygen atom in the ring, phenyl-C₁-C₄-alkyl in which the phenyl ring is optionally substituted by one or two substituents selected from C₁-C₄-alkoxy, amino, C₁-C₄-alkylcarbonylamino, chlorine, bromine, C₁-C₄-alkylsulfonylamino, or di(C₁-C₄-alkyl)aminosulfonylamino and is optionally fused to a 5- membered heterocyclic ring having two oxygen atoms in the ring,

R³ is hydrogen or C₁-C₄-alkyl,

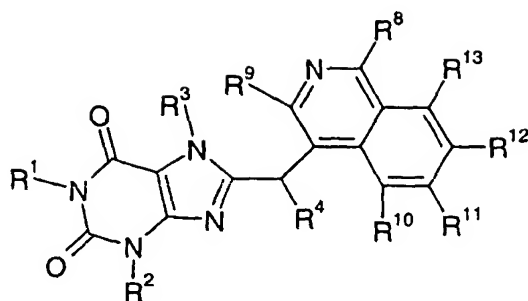
R⁴ is hydrogen or C₁-C₄-alkyl,

R⁵ is a quinolinyl group of formula II, an isoquinolinyl group of formula III or an oxodihydroisoquinolinyl group of formula IIIA, where R⁸, R⁹, R¹⁰, R¹¹, R¹² and R¹³ are each independently selected from hydrogen, halogen, cyano, carboxy, hydroxy, C₁-C₄-alkyl, hydroxy-C₁-C₄-alkyl, C₁-C₄-alkoxy-C₁-C₄-alkyl, C₁-C₄-alkylthio-C₁-C₄-alkyl, C₁-C₄-alkoxy, C₁-C₄-alkylthio, C₂-C₄-alkenyl, C₂-C₄-alkynyl, C₁-C₄-alkylcarbonyl, a group -N(R⁶)R⁷ or phenyl optionally substituted by one or two substituents selected from halogen or C₁-C₄-alkoxy, or R¹¹ and R¹² together with the carbon atoms to which they are attached denote a 5-membered heterocyclic group having two oxygen atoms in the ring, and

R⁶ and R⁷ are each independently hydrogen or C₁-C₄-alkyl optionally substituted by hydroxy or alkoxy or one of R⁶ and R⁷ is hydrogen and the other is C₁-C₄-alkylcarbonyl, or R⁶ and R⁷ together with the nitrogen atom to which they are attached denote a 6-membered heterocyclyl group having one or two nitrogen atoms, or one nitrogen atom and one oxygen atom, in the ring.

5. A compound according to claim 4, in which R⁵ is an isoquinolinyl group of formula III in which R⁸ is hydrogen, C₁-C₄-alkyl, halogen, cyano, -N(R⁶)R⁷ where R⁶ and R⁷ are each independently C₁-C₄-alkyl or R⁶ and R⁷ together with the nitrogen atom to which they are attached denote a 6-membered heterocyclyl group having one or two nitrogen atoms, or one nitrogen atom and one oxygen atom, in the ring, or phenyl substituted by one or two C₁-C₄-alkoxy groups; R⁹ and R¹⁰ are each independently hydrogen, C₁-C₄-alkyl or halogen; R¹¹ and R¹² are each independently hydrogen, halogen, cyano, carboxy, hydroxy, C₁-C₄-alkyl, C₁-C₄-alkoxy or C₂-C₄-alkynyl, or R¹¹ and R¹² together with the carbon atoms to which they are attached denote a 5-membered heterocycle having two oxygen atoms in the ring; and R¹³ is hydrogen or halogen.

6. A compound of formula XXXXVI



XXXXVI

in free or salt form, where

- (i) R^1 is CH_3 , R^2 is $(\text{CH}_3)_2\text{CHCH}_2$, R^3 and R^4 are each H, R^8 is CH_3 , R^9 and R^{10} are each H, and R^{11} and R^{12} are each OCH_3 ; or
- (ii) R^1 is CH_3 , R^2 is $(\text{CH}_3)_2\text{CHCH}_2$, R^3 , R^4 , R^8 , R^9 and R^{10} are each H, and R^{11} and R^{12} are each OCH_3 ; or
- (iii) R^1 is CH_3 , R^2 is $(\text{CH}_3)_3\text{CCH}_2$, R^3 , R^4 , R^8 , R^9 and R^{10} are each H, and R^{11} and R^{12} are each OCH_3 ; or
- (iv) R^1 is CH_3 , R^2 is $(\text{CH}_3)_2\text{CHCH}_2$, R^3 , R^4 , R^9 and R^{10} are each H, R^8 is Cl and R^{11} and R^{12} are each OCH_3 ; or
- (v) R^1 is CH_3 , R^2 is $(\text{CH}_3)_2\text{CHCH}_2$, R^3 , R^4 , R^8 , R^9 and R^{10} are each H, R^{11} is OCH_3 and R^{12} is H; or
- (vi) R^1 is CH_3 , R^2 is cyclopropylmethyl, R^3 , R^4 , R^8 , R^9 , R^{10} and R^{12} are each H and R^{11} is OCH_3 ; or
- (vii) R^1 is CH_3 , R^2 is $(\text{CH}_3)_2\text{CHCH}_2$, R^3 , R^4 , R^8 , R^9 , R^{10} and R^{12} are each H and R^{11} is $\text{CH} \equiv \text{C}$; or
- (viii) R^1 is CH_3 , R^2 is 4-(N-dimethylaminosulfonylamino)benzyl, R^3 , R^4 , R^8 , R^9 and R^{10} are each H and R^{11} and R^{12} are each OCH_3 ; or
- (ix) R^1 is CH_3 , R^2 is $\text{HOCH}_2\text{CH}(\text{CH}_3)\text{CH}_2$, R^3 , R^4 , R^8 , R^9 and R^{10} are each H and R^{11} and R^{12} are each OCH_3 ; or
- (x) R^1 is CH_3 , R^2 is 1-methylcyclopropylmethyl, R^3 , R^4 , R^8 , R^9 and R^{10} are each H and R^{11} and R^{12} are each OCH_3 .

7. A compound according to any one of claims 1 to 6 for use as a pharmaceutical.

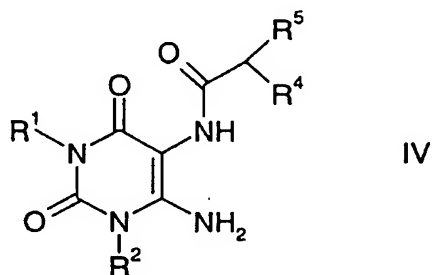
8. A pharmaceutical composition comprising as active ingredient a compound according to any one of claims 1 to 6, optionally together with a pharmaceutically acceptable diluent or carrier.

9. The use of a compound according to any one of claims 1 to 6 for the manufacture of a medicament for the treatment of a condition mediated by PDE5.

10. The use of a compound according to any one of claims 1 to 6 for the manufacture of a medicament for the treatment of sexual dysfunction, particularly male erectile dysfunction.

11. A process for the preparation of a compound of formula I in free or salt form which comprises

1) (a) dehydrating a compound of formula



where R^1 , R^2 , R^4 and R^5 are as defined in claim 1; or

(b) for the preparation of a compound of formula I in free or salt form where R^3 is alkyl optionally substituted by hydroxy, alkoxy or alkylthio, reacting a compound of formula I in free or salt form with an appropriate alkylating agent; or

(c) for the preparation of a compound of formula I in free or salt form where R^2 is aralkyl substituted in the aryl ring by alkylsulfonylamino or dialkylaminosulfonylamino, reacting a compound of formula I in salt form where R^2 is aralkyl substituted by amino with, respectively, an alkylsulfonyl halide or dialkylaminosulfonyl halide; or

(d) for the preparation of a compound of formula I in free or salt form where R^2 is hydroxy-substituted alkyl, hydration of a compound of formula I where R^2 is alkenyl; or

(e) for the preparation of a compound of formula I in free or salt form where R^2 is alkyl substituted by alkylcarbonyloxy, appropriate esterification of a compound of formula I where R^2 is hydroxy-substituted alkyl; or

(f) for the preparation of a compound of formula I in free or salt form where R^2 is aralkyl substituted in the aryl ring by amino, hydrolysing a compound of formula I where R^2 is aralkyl substituted in the aryl ring by acylamino; or

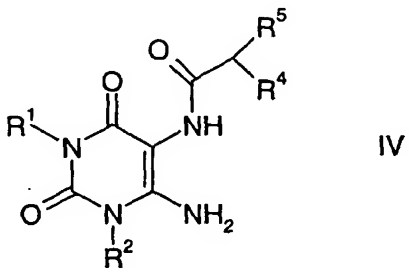
(g) for the preparation of a compound of formula I in free or salt form where R^5 is quinolinylnyl or isoquinolinylnyl substituted by hydroxy, dealkylation of a compound of formula I where R^5 is respectively quinolinylnyl or isoquinolinylnyl substituted by alkoxy; or

(h) for the preparation of a compound of formula I in free or salt form where R^5 is quinolinylnyl or isoquinolinylnyl substituted by halogen, halogenation of a compound of formula I where R^5 is respectively quinolinylnyl or isoquinolinylnyl having an unsubstituted ring carbon atom available for halogenation; or

(i) for the preparation of a compound of formula I in free or salt form where R^2 is a cyclopropyl group, optionally substituted by alkyl, subjecting a compound of formula I where R^2 is alkenyl to a Simmons Smith cyclopropanation reaction; and

2) recovering the resulting product of formula I in free or salt form.

12. A compound of formula IV



where R^1 , R^2 , R^4 and R^5 are as defined in claim 1.